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TRANSMITTAL FORM

(To be used for all correspondence after initial filing)

Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Group Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket No.	59516-147/PP-16093.002

ENCLOSURES (*check all that apply*)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Response
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement; Form PTO-1449
- ☐ Cited References
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts under 37 C.F.R. 1.52 or 1.53
- ☐ Response to Missing Parts/Incomplete Application
- ☐ Drawing(s)
- ☐ Request for Corrected Filing Receipt
- ☐ Licensing-related Papers
- ☒ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation, Change of Correspondence Address
- ☐ Declaration
- ☐ Statement under 37 CFR 3.73(b)
- ☐ Terminal Disclaimer
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- ☐ Request for Refund
- ☐ CD(s), Number of CD(s)
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Return Receipt Postcard
- ☒ Additional Enclosure(s) *(please identify below)*:

Copies of all Office Actions and Responses to Office Actions from October 1, 2002 through November 4, 2004

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Individual Name	Jane E. R. Potter, Registration No. 33,332	27476
Signature	Jane E R Potter	
Date	November 19, 2004	

CERTIFICATE OF FACSIMILE TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date specified below.

Typed or printed name	Jessica Gaunt	
Signature	Jessica Gaunt	Date: November 19, 2004

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PATENT

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November 19, 2004
Date

Jessica Gaunt

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Tian-QiangSun et al.
Application No.	:	09/919,585
Filed	:	July 30, 2001
For	:	ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES

Examiner	:	Richard G. Hutson
Art Unit	:	1652
Docket No.	:	59516-147/PP-16093.002
Date	:	November 19, 2004

Commissioner for Patents
P.O. Box 1450
Alexander, VA 22313-1450

PETITION UNDER 37 C.F.R § 1.181(a)(3)

Sir:

Applicants submit this petition in order to invoke the supervisory authority of the Director. Specifically, applicants request that the Examiner enter the amendment filed on August 19, 2004 and allow claims 1-6, for the reasons discussed herein. Alternatively, applicants request that the Examiner withdraw the finality of the previous Office Action, enter the amendment filed on August 18, 2004, conduct a search of the full pending and elected subject matter, and issue a Notice of Allowance or a non-final action. This petition is believed to

be the proper procedure for addressing this issue, but if a Petition Under 37 C.F.R. § 1.182 is appropriate, the fee of $130 may be charged to Deposit Account No. 04-0258.

STATEMENT OF THE FACTS

Applicants filed this application on July 30, 2001, claiming the benefit of provisional application 60/221,860, which was filed on July 28, 2000. The present application claims and recites polynucleotides and polypeptides of specific SEQ ID NOs, and was filed with 25 claims. In a restriction requirement dated October 1, 2002, the Examiner required restriction to one of the following inventions under 35 U.S.C. § 121:

I. Claims 1-6, drawn to an isolated nucleic acid vector and host cells comprising said nucleic acid and methods of expression of said nucleic acid, classified in class 435, subclass 194.

II. Claims 7, 8, 9, 11 and 12, drawn to kinase polypeptides, classified in class 435, subclass 194.

III. Claim 10, drawn to an antibody against a kinase polypeptide, classified in class 530, subclass 387.1.

IV. Claim 13, drawn to a method of identifying an inhibitor or an enhancer of PAR-1, classified in class 435, subclass 69.1.

V. Claims 14-20, drawn to a PAR-1 modulator, classified in class 514, subclass 789.

VI. Claims 21-25, drawn to a method of treating a mammal with a disease associated with PAR-1, comprising administering a PAR-1 modulator, classified in class 514, subclass 789.

The Examiner also required applicants to select from one of groups A, B, C, and D as indicated at page 3 of the restriction requirement. Each of groups A, B, C, and D includes a polynucleotide and a polypeptide encoded by the polynucleotide of that group. Thus, each of A, B, C, and D recites two related sequences:

A. SEQ ID NO:1 or a sequence encoding SEQ ID NO:3.

B. SEQ ID NO:4 or a sequence encoding SEQ ID NO:6.

C. SEQ ID NO:7 or a sequence encoding SEQ ID NO:9.

D. SEQ ID NO:10 or a sequence encoding SEQ ID NO:12.

It is important to note that the Examiner did not at any time require further restriction or species election of either of the two sequences listed in each of groups A, B, C, and D.

On April 1, 2003, applicants timely responded to the restriction requirement. Applicants elected Group I, directed to nucleic acid vectors, host cells, and methods of expressing the nucleic acid, and applicants also elected the sequences of Group B.

On May 6, 2003, the Examiner issued a first Office Action and specifically acknowledged the election of Group I (claims 1-6) and Group B "SEQ ID NO:4/6" (page 2, line 4). In this Office Action, the Examiner did not indicate that any further election of one sequence from among SEQ ID NO:4 and 6 was required, so applicants reasonably believed that this Office Action was based on a search and analysis of the elected group in full. The grounds of the rejection in the Office Action suggest that the Examiner did consider and search both SEQ ID NO:4 and SEQ ID NO:6. For example, at page 3, for the rejections under 35 U.S.C. § 112, the Examiner discussed language of claim 1, parts (c) and (d), which specifically recited SEQ ID NO:6. On page 4, the rejection under 35 U.S.C. § 112, first paragraph, refers to claims 1 through 6 and mentions issues relating to SEQ ID NO:4. Both SEQ ID NO:6 and SEQ ID NO:4 are further discussed at pages 5, 6, 7, and 8 of the Office Action.

At page 9 of the Office Action, a rejection under 35 U.S.C. § 102(b) was made for claims 1-6. The Examiner stated that the polynucleotide disclosed in the cited art (Espinosa et al.) had a local similarity score of greater than 92% when compared to the sequence of SEQ ID NO:4. The Examiner concluded that Espinosa anticipated claims 1-6.

In a response timely filed on August 6, 2003, applicants amended claim 1 to delete reference to any sequences other than the two elected sequences, specifically SEQ ID NO:6 and SEQ ID NO:4. Subsections (c) and (d) of claim 1 as originally filed were relabeled as subsections (a) and (b) because original subsections (a) and (b) were deleted as they referred to SEQ ID NO:3. Thus, claim 1 as it presently reads contains the same reference to SEQ ID NO:6 as was found in original claim 1 as filed. Applicants also sought to overcome the 35 U.S.C. § 112 rejections by amending claim 1 to recite a biological activity of sequences having the specified percent identity to SEQ ID NO:6 and portions thereof. Applicants also argued that claims 1-6 as amended were not subject to the rejection under 35 U.S.C. § 102(b) over Espinosa.

On October 15, 2003, the Examiner issued a communication indicating that the amendment to claim 1 did not conform to the current rules for claim amendment format. On November 21, 2003, applicants submitted a response in which claim 1 was amended in the proper format. On April 20, 2004, the Examiner issued a final Office Action. The amendment

was entered, but the Examiner maintained the rejections of claims 1-6 under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 112, first paragraph. The Examiner also indicated that claims 1-6 were rejected under 35 U.S.C. § 102(b) over Espinosa, the previously cited art. The Examiner responded to applicants' amendment of claim 1 and specifically stated: "Applicants' attention is drawn to amended claim 1 parts (d), (f), (g), (h), (j), and (k), all of which remain anticipated by Espinosa et al." Applicants interpreted this statement to indicate that claim 1, parts (a), (b) and (c) were not anticipated by Espinosa.

In order to advance the prosecution of this application and to obtain allowance of the subject matter that applicants believed to be allowable based on the Examiner's statements, applicants filed a response on August 19, 2004. In this response, claim 1 was amended to only recite previously existing subgroups (a), (b), and (c), which apparently did not "remain" anticipated by the prior art. All other subject matter was deleted from the claim. Thus, claim 1 recited a sequence encoding amino acids from 1 to 691 of SEQ ID NO:6; a sequence encoding amino acids from 2 to 691 of SEQ ID NO: 6; and complements of the sequences of (a) and (b). This subject matter was the same as subject matter that continuously existed in claim 1 from the time of filing the application through the current status of the application. This subject matter (SEQ ID NO:6) was also specifically elected in response to the original restriction requirement, and at no time did the Examiner require applicants to select from between SEQ ID NO:4 and SEQ ID NO:6. As discussed above, the Examiner acknowledged the election of "SEQ ID NO:4/6." Thus, there has been repeated action by the Examiner clearly suggesting that the entire elected subject matter had in fact been searched, as it properly should have been.

In response to applicants' amendment filed on August 19, 2004, the Examiner issued an Advisory Action dated October 13, 2004 and stated that the proposed amendment of claim 1 deleting the recitation of SEQ ID NO:4, if entered, would result in further search. The amendment was not entered. Applicants' representative conducted a telephone conference with the Examiner on November 3, 2004, and requested an explanation of why a further search should be required when the SEQ ID NO:6 subject matter had existed in the claims from the very beginning and had been specifically elected and acknowledged by the Examiner in response to the restriction requirement.

In reply, the Examiner stated that when the original search was performed, he believed that he had searched SEQ ID NO:4 only, and as soon as art was found, he did not search further.

On November 5, 2004, the Examiner issued a communication with a summary of the telephone interview of November 3, 2004. The Examiner characterized the subject matter of SEQ ID NO:6 as a "sub-genus." The Examiner stated that because the "genus" of SEQ ID NO:6 and SEQ ID NO:4 had been searched, and art reading on the genus had been found, cancellation of the subject matter of SEQ ID NO:4 would cause a further search of the sub-genus (SEQ ID NO:6). Applicants submit that there is nothing in the prosecution history prior to the November 5, 2004 communication that suggests a genus/sub-genus relationship between a polynucleotide and the polypeptide encoded by that polynucleotide. For this reason, applicants request action by the Director to provide for allowance or further search, whichever is appropriate on the record, as discussed below.

ACTION REQUESTED

Applicants request, as a first alternative, that the Examiner indicate on the record that claim 1 is allowable over the cited art. The conclusion seems to be implicit in the Examiner's statement in the Office Action dated April 20, 2004 at page 9:

> Applicants' comments are noted, however, the rejection remains. Applicants' attention is drawn to amended claim 1 parts (d), (f), (g), (h), (j) and (k) . . . all of which remain anticipated by Espinosa et al.

If the entirety of claim 1 was anticipated by Espinosa, it seems that there would be no need to specify certain parts that remained anticipated following entry of an amendment. Applicants therefore were justified in relying on the unlisted parts (claim 1(a), (b), and (c)) as not being anticipated by the cited art. Applicants submit that the Examiner has made an *ad hoc* request for a species election, which is not appropriate at this time in the prosecution. In the absence of a species election in the original restriction requirement dated October 1, 2002, the Examiner should have conducted a full range search after applicants responded to the restriction requirement by selecting sequences of Group B, SEQ ID NO:4 and SEQ ID NO:6, which, as indicated above, are related sequences. The Examiner subsequently acknowledged election of both sequences when he referred to elected SEQ ID NO:4/6. The current elements (a), (b) and (c) of claim 1 were in claim 1 as of the filing date of the application, as elements 1(c), (d) and (i). The designation of these elements only changed to (a), (b) and (c) because claim 1 was amended to delete reference to SEQ ID NOs that were not elected in response to the restriction requirement. At this stage in the prosecution, it is inappropriate and outside the Examiner's

authority to assert that a new search is necessitated. Applicants submit that the Examiner should have completed a full range search between the date of the restriction requirement response and the first Office Action. To support the arguments herein, applicants have submitted copies of the relevant Office Actions and Responses as Exhibits.

In the alternative, if the Examiner cannot document that SEQ ID NO:6 was searched following its election on April 1, 2003, applicants hereby request that the Examiner perform a search and issue a non-final Office Action or a Notice of Allowance.

To the extent that the prosecution of this application extends beyond three years from filing to issue, applicants request that the patent term be extended as appropriate to restore any term lost due to the Examiner's failure to search the properly elected subject matter. By relying on the Examiner's representation that the elected subject matter had been searched, when in fact it has not been, applicants lost the opportunity to timely respond to any issues that such a search might have raised.

Applicants also request refund of the fee paid to file the Notice of Appeal on August 19, 2004. The Notice of Appeal was filed for the sole purpose of maintaining pendancy while the issue relating to the failure to examine the full subject matter, as discussed herein, is resolved.

Kindly charge any amounts required for this Petition to Deposit Account No. 04-0258 of Davis Wright Tremaine LLP. This page is included in duplicate.

Respectfully submitted,
Tian-Qiang Sun et al.
DAVIS WRIGHT TREMAINE LLP

By 
Jane E. R. Potter
Registration No. 33,332

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,585	07/30/2001	Tian-Qiang Sun	PP-16093.002	2590

7590 10/01/2002

Chiron Corporation
Intellectual Property R338
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETED on/by 10/7/02 GM
Atty. AGD PA
File # PP16093.002
Due Date 11/1/02 Ext R/05
Final Date 4/1/03 RQ

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 09/919,585	Applicant(s) SUN ET AL.	
	Examiner Richard G Hutson	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-25 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, drawn to an isolated nucleic acid vector and host cells comprising said nucleic acid and methods of expression of said nucleic acid, classified in class 435, subclass 194.

II. Claims 7, 8, 9, 11 and 12, drawn to kinase polypeptides, classified in class 435, subclass 194.

III. Claim 10, drawn to an antibody against a kinase polypeptide, classified in class 530, subclass 387.1.

IV. Claim 13, drawn to a method of identifying an inhibitor or an enhancer of PAR-1, classified in class 435, subclass 69.1.

V. Claims 14-20, drawn to a PAR-1 modulator, classified in class 514, subclass 789.

VI. Claims 21-25, drawn to a method of treating a mammal with a disease associated with PAR-1, comprising administering a PAR-1 modulator, classified in class 514, subclass 789.

For each of inventions I-VI above, restriction to one of the following is also required under 35 USC 121. Therefore, election is required of one of inventions I-VI and one of inventions (A)-(D).

(A). SEQ ID NO: 1 or a sequence encoding SEQ ID NO: 3.

(B). SEQ ID NO: 4 or a sequence encoding SEQ ID NO: 6.

(C). SEQ ID NO: 7 or a sequence encoding SEQ ID NO: 9.

(D). SEQ ID NO: 10 or a sequence encoding SEQ ID NO: 12.

The inventions are distinct, each from the other because of the following reasons:

Inventions (A)-(D) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, represent structurally different polypeptides and the polynucleotides encoding them. Therefore, where structural identity is required, such as for hybridization or expression, the different sequences have different effects.

Inventions I-III and V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the nucleic acid of Group I, the polypeptide of Group II, the antibody of Group III and the PAR-1 modulator of Group V each comprise a chemically unrelated structure capable of separate manufacture, use and effect. The polypeptides of Groups I and IIII each comprise a different amino acid sequence and the nucleic acid of Group I is comprised of nucleic acid sequence. The Par-1 modulator of Group V is not defined structurally although may be an oligonucleotide, ribozyme, protein, polypeptide or small molecule, each of which is distinct from Groups I-III. The nucleic acid has other utility

besides encoding protein such as a hybridization probe, and the proteins can be made synthetically. Additionally, the proteins can be used to perform specific biological function(s) which are independent of the function(s) of the DNA molecule.

Inventions I and IV are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the nucleic acid of Group I can be used in a materially different process such as one in which the nucleic acid is used in a diagnostic hybridization assay.

The protein of Group II, the antibody of Group III, and the modulator of Group V are unrelated to the method of Group IV as they are neither used nor made by the method of Group IV.

Inventions V and VI are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the modulator of Group V can be used in a materially different process such as one in which the modulator is used in a method of characterizing the PAR-1 polypeptide and its interaction with other polypeptides.

The nucleic acid of Group I, the protein of Group II and the antibody of Group III, are unrelated to the method of Group VI as they are neither used nor made by the method of Group VI.

The methods of Groups IV and VI are independent as they comprise different steps, utilize different products and produce different results.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the literature and sequence searches required for each of the Groups are not required for another of the Groups, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
September 30, 2002

Attorney Docket No. 59516-147 Chiron
Date mailed: April 1, 2003 via Express Mail Label EV284452609US
Please advise serial number

Please acknowledge receipt of the following:

1. Transmittal Form
2. Fee Transmittal Form in duplicate
3. Check in the amount of $930
4. Request for Three-Month Extension of Time in duplicate
5. Response to Restriction Requirement
6. Postcard indicating receipt

Thank you.

DAVIS WRIGHT TREMAINE LLP

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SEATTLE, WASHINGTON 98101-1688
(206) 622-3150

Bank of America
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Asheville, North Carolina

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DATE APRIL 01, 2003

PAY DAVIS, WRIGHT $930dol's00cts DOLLARS $ 930.00

TO THE ORDER OF
COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231

DAVIS WRIGHT TREMAINE LLP

BY

Checks Exceeding $50,000 Require Two Signatures

11067 ⑈00544850⑈ ⑆053107989⑆ 0004801206 10⑈

Attorney Docket No. 59516-147 Chiron
Date mailed: April 1, 2003 via Express Mail Label EV284452609US
Please advise serial number

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EV284452609US

Thank you.

EXPRESS MAIL NO. EV284452609US

PTO/SB/21 (01-03)
Approved for use through 04/03/2003. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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TRANSMITTAL FORM

(To be used for all correspondence after initial filing)

Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Sun
Group Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket No.	59516-147

ENCLOSURES (*check all that apply*)

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- [X] Additional Enclosure(s) *(please identify below)*:

Response to Restriction Requirement_____

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Individual Name	Barry L. Davison
Signature	
Date	April 1, 2003

22504
PATENT TRADEMARK OFFICE

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on the date specified below.

Typed or printed name		
Signature		Date:

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, Washington, D.C. 20231.**

PTO/SB/17 (10-02)
Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 930

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Sun
Examiner Name	Richard G. Hutson
Art Unit	1652
Attorney Docket No.	59516-147

METHOD OF PAYMENT *(check all that apply)*

☒ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 04-0258

Deposit Account Name: Davis Wright Tremaine LLP

The Commissioner is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☒ Credit any overpayments

☒ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	740	2001	370	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	510	2003	255	Plant filing fee	
1004	740	2004	370	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X =
Independent Claims		- 3** =		X =
Multiple Dependent				=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	400	2252	200	Extension for reply within second month	
1253	920	2253	460	Extension for reply within third month	930
1254	1,440	2254	720	Extension for reply within fourth month	
1255	1,960	2255	980	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,280	2453	640	Petition to revive - unintentional	
1501	1,280	2501	640	Utility issue fee (or reissue)	
1502	460	2502	230	Design issue fee	
1503	620	2503	310	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	740	2809	370	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	740	2810	370	For each additional invention to be examined (37 CFR 1.129(b))	
1801	740	2801	370	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 930

SUBMITTED BY

(Complete *(if applicable)*)

Name *(Print/Type)*	Barry L. Davison	Registration No. *(Attorney/Agent)*	47,309	Telephone	(206) 628-7621
Signature				Date	April 1, 2003

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

EXPRESS MAIL NO. EV284452609US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Sun et al.
Application No.	:	09/919,585
Filed	:	July 30, 2001
For	:	ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES

Examiner	:	Richard G. Hutson
Art Unit	:	1652
Docket No.	:	59516-147/ PP-16093.002
Date	:	April 01, 2003

Box Non Fee Amendment
Commissioner for Patents
Washington, DC 20231

REQUEST FOR THREE-MONTH EXTENSION OF TIME

Sir:

Applicants respectfully request a three-month extension of time for response to the outstanding Restriction Requirement dated October 1, 2002 for the above-identified patent application, three months, up to and including April 1, 2003.

Applicants have enclosed a check for $930, which includes the large entity fee. Kindly charge any additional amounts or provide any credits to Deposit Account No. 04-0258 of Davis Wright Tremaine LLP. This page is included in duplicate.

Respectfully submitted,

Nobuyuki Itoh et al.,

Davis Wright Tremaine LLP

Barry L. Davison, Ph.D, J.D.
Registration No. 47,309 for

Janer E. R. Potter, Ph.D., J.D.
Registration No. 33, 332

EXPRESS MAIL NO. EV284452609US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Sun et al.
Application No.	:	09/919,585
Filed	:	July 30, 2001
For	:	ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES

Examiner	:	Richard G. Hutson
Art Unit	:	1652
Docket No.	:	59516-147/ PP-16093.002
Date	:	April 01, 2003

Box Non Fee Amendment
Commissioner for Patents
Washington, DC 20231

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

This is in response to a Restriction Requirement dated 01 October 2002 for the above-identified patent application. A shortened statutory period for reply was set to expire 3 months from 01 October 2002. Applicants attach a Request for a 3-month Extension of Time up to and including 01 April 2003, along with a check to cover the requisite fee.

REMARKS

The invention has been restricted into six claim groups (I-VI), and further into four sequence groups (A-D), whereby election of one of group I-VI, and one of group A-D is required.

Applicants elect group I directed to nucleic acid vectors, host cells comprising same and methods of expression of said nucleic acid, and group (B) comprising nucleotide sequence SEQ ID NO:4 and amino acid sequence SEQ ID NO:6 without traverse.

Applicants respectfully request examination and consideration of claims 1-6 in view of the elected invention.

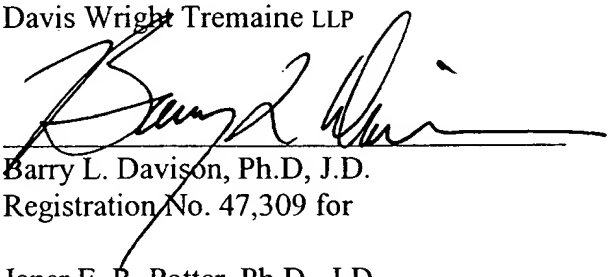
Respectfully submitted,

Nobuyuki Itoh et al.,

Davis Wright Tremaine LLP

22504

PATENT TRADEMARK OFFICE



Barry L. Davison, Ph.D, J.D.
Registration No. 47,309 for

Janer E. R. Potter, Ph.D., J.D.
Registration No. 33, 332

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,585	07/30/2001	Tian-Qiang Sun	PP-16093.002	2590

7590 05/06/2003

Chiron Corporation
Intellectual Property R338
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	31

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/919,585	SUN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claims 1-25 are at issue and are present for examination.

Election/Restrictions

Applicant's election without traverse of Group I and Group B, SEQ ID NO: 4/6, Claims 1-6, in Paper No. 7 is acknowledged.

Claims 7-25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

Applicants statement on the first line of the specification to state that this application claims the priority of U.S. Provisional Application Number 60/221,860, filed July 28, 2000 where this provisional application is incorporated by reference is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure, paper no. 4, filed 1/10/2002, is acknowledged. Those references considered have been initialed.

Claim Objections

Claims 1-6 are objected to because of the following informalities:

Claims 1 (2-6 dependent from) contains non-elected subject matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-6 dependent on) is indefinite in that it is vague and confusing in the recitation in part (c) "...amino acids from about 1 to about 691 of SEQ ID NO: 6" and in part (d) "...amino acids from about 1 to about 691 of SEQ ID NO: 6". Specifically the use of "about" when referring to an amino acid position is vague and indefinite. What is applicants intent in reference to about 1 or about 2, and are they different? It is suggested that the word "about" be deleted from the above recitations.

Claim 1 (2-6 dependent on) is indefinite in that it is vague and confusing in the recitation in part (s) "...except for a conversion of a conserved lysine to an alanine at an

ATP binding site of the encoded amino acid sequence". It is vague and unclear what applicants consider to be an ATP binding site of the sequences of (c) and (d) (i.e. SEQ ID NO: 6).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6 are directed to all possible nucleic acid molecules comprising any polynucleotide having (comprising) a sequence having a mere 50, 100 or 500 contiguous nucleotides from the coding region of SEQ ID NO: 4 (part k, o and p); any polynucleotide having (comprising) sequences having at least 90% identity to the above (k) or to a sequence encoding amino acids 1-691 of SEQ ID NO: 6; and sequences of (c) except at least one amino acid substitution in the encoded amino acid sequence; and vectors and host cells comprising said nucleic acid molecules and methods of making said vectors and host cells.

The specification, however, only provides the representative species of SEQ ID NO: 4, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also

fails to describe additional representative species of these nucleic acid molecules by any identifying structural characteristics or properties other than the defined relationship to SEQ ID NO: 4 or 6, for which limited predictability is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. Applicant is advised to in addition to more structural detail, adding functional language to the rejected claims such that an adequate structure to function/activity relationship of the claimed genus is described.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising a polynucleotide sequence encoding SEQ ID NO: 6, does not reasonably provide enablement for any nucleic acid molecule comprising a polynucleotide sequence at least 90% identical to a sequence encoding SEQ ID NO: 6, or sequence that is a mere 50, 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, or any sequence except for at least one amino acid substitution in the encoded amino acid sequence. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-6 are so broad as to encompass any nucleic acid molecule comprising any polynucleotide having (comprising) a sequence having a mere 50, 100 or 500 contiguous nucleotides from the coding region of SEQ ID NO: 4 (claim 1, part k, o and p); any polynucleotide having (comprising) sequences having at least 90% identity to the above (claim 1, part n) or to a sequence encoding amino acids 1-691 of SEQ ID NO: 6; and sequences of (c) except at least one amino acid substitution in the encoded amino acid sequence (claim 1, part r); and vectors and host cells comprising said nucleic acid molecules and methods of making said vectors and host cells.. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid molecules broadly encompassed by the claims, including all nucleic acid molecule comprising a polynucleotide sequence at least 90% identical to a mere 50 contiguous nucleotides of a sequence encoding SEQ ID NO: 6,. The claims rejected under this section of U.S.C. 112, first paragraph,

do not place minor structural limits on the claimed nucleic acid molecules such that adequate guidance is not disclosed with respect to how to make and use the majority of the scope of the claimed genus. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and thus its encoding nucleic acid's sequence and obtain the desired function or activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that nucleic acid molecule comprising a polynucleotide sequence encoding SEQ ID NO: 6.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's or polynucleotide's sequence where modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any nucleic acid molecule comprising a polynucleotide sequence at least 90% identical to a sequence encoding SEQ ID NO: 6,

or sequence that is a mere 50, 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, because the specification does not establish: (A) regions of the protein and thus polynucleotide structure which may be modified without effecting its activity; (B) the general tolerance of serine/threonine protein kinases and their encoding polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a serine/threonine protein kinases with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain a function/activity of the claimed polynucleotides or their encoded polypeptides and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at and use the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any polynucleotide encoding SEQ ID NO: 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24

(CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Espinosa et al., (Human serine/threonine protein kinase EMK1: genomic structure and cDNA cloning of isoforms produced by alternative splicing, Cytogenet. Cell Genet., Vol 81, No 3/4, pages 278-282, 1998, Ref V, enclosed 892) as evidenced by Espinosa et al. (Genbank Accession Number X97630, October 1998).

Espinosa et al. teach isolation and cloning of a polynucleotide that encodes two isoforms of the human serine/threonine protein kinase EMK1 and Espinosa et al. teach vectors and host cells comprising said polynucleotide and methods of making said vectors and host cells. The polynucleotide isolated, cloned and disclosed by Espinosa et al. has a best local similarity score of greater then 92% when compared to the sequence of SEQ ID NO: 4 and the taught nucleic acid comprises polynucleotide

sequences of at least 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, as evidenced by Espinosa et al. (Genbank Accession Number X97630, October 1998).

Therefore, Espinosa et al. anticipates claims 1-6.

Remarks

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Primary Patent Examiner
Art Unit 1652
May 2, 2003

Express Mail No. EL852691657US

JEF:jeh

59516-147/PP-16093.002

SENT: AUGUST 6, 2003

DUE: August 6, 2003

Date Stamp

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Kindly acknowledge receipt of the below-listed documents by placing your receiving stamp hereon and mailing:

1. PTO/SB/21 Transmittal
2. PTO/SB/17 Fee Transmittal (+1 copy)
3. Response to Office Action dated May 6, 2003
4. Information Disclosure Statement
5. PTO/SB/08
6. Cited Reference (10)

In Re: Tian-Qiang Sun et al.; **for;** ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES ; **Filed:** July 30, 2001; **as USAN:** 09/919,585

DAVIS WRIGHT TREMAINE LLP

Express Mail No. EL852691657US

JEP:jen
Docket No.: 59516-147/PP-16093.002

SENT: AUGUST 6, 2003
DUE: August 6, 2003

Date Stamp

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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In Re: Tian-Qiang Sun et al.; **for;** ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES ; **Filed:** July 30, 2001; **as USAN:** 09/919,585

DAVIS WRIGHT TREMAINE LLP

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59516-147/PP-16093.002
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TRANSMITTAL FORM

(To be used for all correspondence after initial filing)

Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Group Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket No.	59516-147/PP-16093.002

ENCLOSURES (*check all that apply*)

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [X] Amendment/Response
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [X] Information Disclosure Statement; Form PTO/SB/08
- [X] Cited References (10)
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts under 37 C.F.R. 1.52 or 1.53
- [ ] Response to Missing Parts/Incomplete Application
- [ ] Drawing(s)
- [ ] Request for Corrected Filing Receipt
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation, Change of Correspondence Address
- [ ] Declaration
- [ ] Statement under 37 CFR 3.73(b)
- [ ] Terminal Disclaimer
- [ ] Small Entity Statement
- [ ] Request for Refund
- [ ] CD(s), Number of CD(s)
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Individual Name	Jane E. R. Potter, Registration No. 33,332	27476 PATENT TRADEMARK OFFICE
Signature		
Date	August 6, 2003	

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FEE TRANSMITTAL for FY 2003

Effective 01/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 180

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Examiner Name	Richard G. Hutson
Art Unit	1652
Attorney Docket No.	59516-147/PP-16093.002

METHOD OF PAYMENT *(check all that apply)*

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FEE CALCULATION

1. **BASIC FILING FEE**

Large Entity Fee Code	Large Entity Fee($)	Small Entity Fee Code	Small Entity Fee($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. **EXTRA CLAIM FEES**

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20** =		x		=	
Independent Claims		- 3** =		x		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** *Reissue independent claims over original patent*
1205	18	2205	9	** *Reissue claims in excess of 20 and over original patent*

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. **ADDITIONAL FEES**

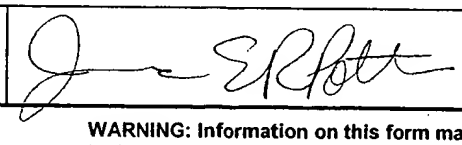
Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,300	2453	650	Petition to revive – unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Petitions related to provisional applications	
1806	180	1806	180	Submission of Information Disclosure Stmt	180
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) ____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 180

SUBMITTED BY

Name (Print/Type) Jane E. R. Potter		Registration No. Attorney/Agent)	33,332
Signature		Date August 6, 2003	

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SEA 1395078v1 59516-147
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Tian-Qiang Sun et al.
Application No.	:	09/919,585
Filed	:	July 30, 2001
For	:	ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES
Examiner	:	Richard G. Hutson
Art Unit	:	1652
Docket No.	:	59516-147 / PP-16093.002
Date	:	August 6, 2003

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE UNDER 37 C.F.R. § 1.112

Introductory Comments

Commissioner for Patents:

This amendment is filed in response to an Office Action dated May 6, 2003, for the above-identified patent application. Applicants submit that no extension of time is required, but if an extension is required, it is hereby petitioned, and the fee may be charged to Deposit Account No. 04-0258.

Amendment to the Claims

1. (Amended) An isolated nucleic acid molecule comprising a polynucleotide having a sequence selected from the group consisting of:

~~(a) a sequence encoding amino acids from about 1 to about 744 of SEQ ID NO:3;~~

~~(b) a sequence encoding amino acids from about 2 to about 744 of SEQ ID NO:3;~~

~~(c)~~ a sequence encoding amino acids from ~~about~~ 1 to ~~about~~ 691 of SEQ ID NO:6;

~~(d)~~(b) a sequence encoding amino acids from ~~about~~ 2 to ~~about~~ 691 of SEQ ID NO:6;

~~(~~

~~e) a sequence encoding amino acids from about 1 to about 724 of SEQ ID NO:9;~~

~~(f) a sequence encoding amino acids from about 2 to about 724 of SEQ ID NO:9;~~

~~(g) a sequence encoding amino acids from about 1 to about 795 of SEQ ID NO:12;~~

~~(h) a sequence encoding amino acids from about 2 to about 795 of SEQ ID NO:12;~~

~~(i)~~(c) complements of the sequences of (a)-~~(h)~~(b);

~~(j) a sequence having 50-2232 contiguous nucleotides from the coding region of SEQ ID NO:1;~~

~~(k)~~(d) a sequence having 50-2073 contiguous nucleotides from the coding region of SEQ ID NO:4;

~~(l) a sequence having 50-2172 contiguous nucleotides from the coding region of SEQ ID NO:7;~~

~~(m) a sequence having 50-2385 contiguous nucleotides from the coding region of SEQ ID NO:10;~~

~~(n)~~(e) sequences having at least ~~90%~~95% identity to the sequences of ~~(a) – (m)~~(b) – (d), wherein the polypeptide encoded by said sequence has kinase activity~~.~~;

~~(o)~~(f) sequences having 100-1500 contiguous nucleotides from the coding region of ~~SEQ ID NO:1,~~ SEQ ID NO:4~~, SEQ ID NO:7 or SEQ ID NO:10~~;

~~(p)~~(g) sequences having 500-1000 contiguous nucleotides from the coding region of ~~SEQ ID NO:1,~~ SEQ ID NO:4~~, SEQ ID NO:7 or SEQ ID NO:10~~;

~~(q)~~(h) sequences of (a) – ~~(h)~~(b)~~, except for at least one amino acid substitution in the encoded amino acid sequence; and~~ wherein said sequence encodes a polypeptide of SEQ ID NO:6 with at least one amino acid substitution, wherein said polypeptide has kinase activity;

~~(r)~~(i) sequences of (a) – ~~(h)~~(b), wherein said sequence encodes a polypeptide of SEQ ID NO:6 with ~~except for~~ a conversion of a conserved lysine to an alanine at an ATP binding site of ~~the encoded amino acid sequence~~ SEQ ID NO:6, wherein said polypeptide has kinase activity.~~;~~

(j) sequences of (f) – (g) wherein said sequence encodes a polypeptide having at least one amino acid substitution compared to the corresponding region of SEQ ID NO:6 encoded by said coding region; and

(k) sequences of (f) – (g) wherein said sequence encodes a polypeptide having a conversion of a conserved lysine to an alanine at an ATP binding site compared to the corresponding region of SEQ ID NO:6 encoded by said coding region.

2. (Original) A method of making a vector comprising inserting a nucleic acid molecule of claim 1 into said vector in operable linkage to a promoter.

3. (Original) A vector produced by the method of claim 2.

4. (Original) A method of making a host cell comprising transforming or transfecting a vector of claim 3 into a cell.

5. (Original) A host cell produced by the method of claim 4.

6. (Original) A method of making a polypeptide, comprising culturing the host cell of claim 5 under conditions such that said polypeptide is expressed and recovering said polypeptide.

7-25. (Withdrawn)

REMARKS

Applicants submit this response to the Office Action of May 6, 2003. As a result of a restriction requirement dated October 1, 2002, the invention has been restricted into six claim groups (I-VI), and further into four sequence groups (A-D), whereby election of one of group I-VI, and one of group A-D was required. Applicants elected group I, directed to nucleic acid vectors, host cells comprising same and methods of expression of the nucleic acid, and group (B) comprising nucleotide sequence SEQ ID NO:4 and amino acid sequence SEQ ID NO:6. As a result, claims 1-6 are pending and claims 7-25 are withdrawn from consideration. Claim 1 is amended to recite the elected sequences, and further amendments are discussed below. The recitation of "95% identity" in claim 1 is supported at least at page 60, lines 7-9 of the specification. No new matter is added.

An Information Disclosure Statement is filed herewith to confirm that the patents and publications intended to be disclosed for the record, and which are cited in the specification, are made of record.

Claims 1-6 are objected to for reciting nonelected subject matter. This has been addressed by amending independent claim 1, from which claims 2-6 depend.

Claims 1-6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Without acquiescing to the ground of rejection, applicants submit that claim 1 as amended is not subject to the specific grounds of objection ("about" language, and "ATP binding site").

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification so as to reasonably convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention. Without acquiescing to the ground of rejection, applicants have amended claim 1, from which claims 2-6 depend. The Examiner recommended adding functional language to the rejected claims (Office Action, page 5, lines 8-9), and the amended claims address this issue. The kinase activity of the polypeptide expressed by the claimed nucleic acid molecule is disclosed in the specification at, for example, page 245, first paragraph and page 247,

lines 10-12. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph (enablement). The Examiner states that the specification is enabling for a nucleic acid molecule comprising a polynucleotide sequence encoding SEQ ID NO:6. However, the specification allegedly is not enabling for any nucleic acid molecule at least 90% identical to a sequence encoding SEQ ID NO:6; a sequence that is 50, 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO:4; or any sequence except for at least one amino acid substitution in the encoded amino acid sequence. The Examiner cited the Wands factors (*In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988)).

A specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a *prima facie* case of lack of enablement. See, In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976); In re Marzocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). To make a *prima facie* case of lack of enablement, the PTO must come forward with reasons, supported by the record as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The mere fact that some experimentation is necessary does not negate enablement as long as undue experimentation is not required. See M.P.E.P. § 608.01(p).

The burden is on the PTO to establish that experimentation would be undue, Angstadt, 190 U.S.P.Q. at 219, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1404 (C.A.F.C. 1988). Applicants submit that the amount of experimentation that may be required to practice the present invention does not rise to the level of being undue experimentation, as defined by the Court in Wands.

An important aspect of the Court's decision in Wands is its finding that the nature of the technology pertinent to the Wands invention (monoclonal antibody production) permitted a broad definition of the term "experiment." The Court found that an "experiment" in the monoclonal antibody art consisted of the entire attempt to make a monoclonal antibody against a

particular antigen. As described by the Court, the process entailed, "immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 8 U.S.P.Q.2d at 1407. Thus, Wands supports the conclusion that, in a complex field such as monoclonal antibody production, the entire attempt to achieve the desired result, from beginning to end, constitutes one experiment.

According to the Court, repetition of this whole experiment more than once does not constitute undue experimentation. As the Court indicated, practitioners in the art would be prepared to screen negative hybridomas in order to find a hybridoma making the desired antibody. 8 U.S.P.Q.2d at 1406. Thus, the fact that some aspects of the experiment as a whole may yield negative results does not mandate a finding that the amount of experimentation to achieve a positive result is undue.

Applying this information to the eight Wands factors, one of skill in the art would conclude that undue experimentation would not be required to practice the claimed invention.

1. *Quantity of experimentation necessary.* Applicants submit that one of ordinary skill in the art can construct a hybridization probe based on the disclosed polynucleotide, SEQ ID NO:6, and use the probe to locate and obtain hybridizing DNA. The polypeptide encoded by the hybridizing DNA would be tested for PAR-1Bα activity (as claimed, kinase activity), and the polynucleotide would be evaluated on the basis of the limitations of the claimed identity with the amino acid sequence of SEQ ID NO:4. If the results of these routine procedures were positive, the polynucleotide sequence would fall within the scope of the claims. Such tests would not constitute "undue" experimentation within the scope of Wands. To determine if a polynucleotide falls within the scope of the claims, the only experimentation required is the performance of transfection and assay procedures. These procedures are routine and would not have to be done repeatedly before a clear result was obtained. Because the inventors and the art provide means for the objective measurement of a polynucleotide falling within the claim scope, this factor is met, for example, by the ability of the polynucleotide to encode a protein capable of blocking the inhibitory activity of mutant Kinase-negative PAR-1 (KN PAR-1). This is described in the specification at pages 246-247.

The Wands court found that practitioners in the art are prepared to screen negative hybridomas to find one that made the desired antibody. (8 USPQ2d at 1406.) The court further stated that an "experiment" was not simply the screening of a single hybridoma, but instead was the entire attempt to make a monoclonal antibody against a particular antigen. This process included immunizing animals, fusing lymphocytes from the immunized animals to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas. (8 USPQ2d at 1406).

By analogy, a single experiment in the present art could include obtaining or constructing a polynucleotide, transfecting it into CHO cells that co-express wild-type PAR-1, and determining if Dvl is phosphorylated. Encountering negative results would not mean that undue experimentation is involved, according to Wands.

2. *Amount of direction or guidance provided.* Like the production of monoclonal antibodies, the identification or production of DNA encoding a polypeptide having PAR-1B α activity and falling within the scope of the claims may require some experimentation, but if viewed in the light of Wands, this experimentation is not undue. The present applicants provide extensive guidance to allow one of ordinary skill in the art to obtain DNA that is within the scope of the claims. The Examiner stated that "it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims..." (Page 7, first full paragraph.) Applicants, first, request that the Examiner provide support for this statement about what is and is not routine in this art. Second, the claims do not require a practitioner in this art to "screen for multiple substitutions or multiple modifications." Instead, the screening would entail testing one or more polypeptides for activity as described in the specification, to determine if a given polynucleotide encodes a polypeptide within the scope of the claims. The specification provides clear directions for performing the procedures, and provides cites to published scientific articles for details not mentioned in the specification. Similarly, the Wands court found that the starting material was available to the public (as is the material used in the present application) and the patent application at issue in Wands provided a detailed description of the methods, which included use of a commercially available kit. (8

USPQ 2d at 1404, 1405). The cell lines used in applicants' methods are commercially available, and the application describes the methods, at pages 245-247.

3. *Presence or absence of working examples*. The specification describes transfection of CHO cells using a claimed polynucleotide of the invention, specifically PAR-1B α. (Page 247, lines 10-11.) The co-expression experiment provides an example that is applicable to other claimed polynucleotides (test polynucleotides), which would be co-expressed in the CHO cells along with the mutant (PAR-1 KN) construct. The blocking of inhibitory effects of PAR-1 KN would signal that the test polynucleotide is within the scope of the claims.

These experiments show that it is routine to detect the effect of PAR-1 inhibition. This can be accomplished by transfecting HT1080 cells with an antisense oligonucleotide, lysing the cells after a period of incubation, and analyzing (a) PAR-1 protein content using antibodies, and (b) activity of a reporter gene, specifically a LEF1 reporter. These experiments provide an objective way of measuring PAR-1 activity. The methods are disclosed in the Sun *et al.* publication. These methods are also disclosed in the present patent application at page 247-248, Example 6.

Example 5 of the application, at pages 246-247, describes experiments in which cDNAs for PAR-1 were transfected into Chinese hamster ovary (CHO) cells. In one set of experiments, cDNAs encoding mutant forms of PAR-1, which did not have kinase activity, were transfected into CHO cells. In the absence of the kinase activity, the target of PAR-1 phosphorylation, Dishevelled (Dvl), is not phosphorylated. This result is detected as a reduced amount of a retarded Dvl band. Importantly for the purposes of this invention, if wild-type PAR-1 (capable of phosphorylating Dsl) is co-expressed with the mutant forms of PAR-1 in the CHO cells, the inhibitory activity of the mutant PAR-1 is blocked. This provides a method for determining if a polynucleotide sequence with a given percent homology to SEQ ID NO:6 is capable of functioning as a wild-type PAR-1 sequence, namely, able to encode functional PAR-1 protein. Such experimentation is routine, as it employs known methods and known materials, and needs only the addition of a test polynucleotide to measure objectively whether the polynucleotide falls within the scope of the claims.

4. *Nature of the invention.* The inventors have, for the first time, identified and cloned a human homologue of the *Drosophila* gene referred to as PAR-1. Three human homologues were identified and cloned, and one, the PAR-1Bα form, is under examination in this application. As discussed in a related publication by the inventors, Sun, Tian-Qiang *et al.*, "PAR-1 is a Disheveled-associated kinase and a positive regulator of Wnt signaling," *Nature Cell Biology* 3:628-636, 2001, PAR-1 plays a role in a pathway referred to as the Wnt pathway. Through a series of receptor interactions, Wnt enhances the ability of a protein to antagonize the activity of glycogen synthase kinase 3β. The effect of this pathway, and the associated interactions of the components, is to stabilize the cytosolic protein β-catenin. β-catenin in turn moves to the nucleus, where it combines with a transcription factor to regulate expression of genes. In humans, abnormalities in regulation of the Wnt pathway can cause cancer, as described below. PAR-1 has been shown by the inventors to modulate this Wnt-β-catenin pathway. Thus, it is an important protein from the perspective of its role in normal cell function, and because the Wnt pathway is implicated in cancer, proteins that play a role in this pathway are also implicated in cancer. Functionally, PAR-1 is a serine-threonine kinase.

The inventors designed and performed experiments to determine how cells would react to inhibition of PAR-1. HT1080 cells were chosen because oligonucleotides such as antisense RNA can be delivered to these cells with relative ease, and because HT1080 has a robust transcriptional response to Wnt, allowing the investigator to detect changes in gene expression resulting from disruption of this pathway. (Sun *et al.*, page 632, left column, lines 10-17.) Antisense oligonucleotides capable of specifically binding to PAR-1 reduced PAR-1 messenger RNA (mRNA) by 75-90%, and also reduced PAR-1 protein levels. The inhibition was accompanied by a reduction in Wnt-induced reporter activity. (Sun *et al.*, page 632, left column, lines 17-20). These results showed that (a) it is possible to connect an inhibition of PAR-1 with processes associated with PAR-1 activity, and (b) it is possible to *selectively* inhibit PAR-1 mRNA levels and protein levels. This selective inhibition is achieved using antisense oligonucleotides that specifically recognize and hybridize with PAR-1 sequences of the invention.

The invention relates to human polynucleotides. Methods of synthesizing, isolating, mutating, manipulating, transfecting, and expressing polynucleotides are the basis of the biotechnology industry. The nature of the invention is such that it is well-known to those of ordinary skill in the art.

5. *The state of the prior art.* The prior art provides the methods and materials needed to apply the methods of factor (4) above to this group of polynucleotides, specifically hPAR-1 polynucleotides. The Wands court found that "all the methods needed to practice the invention were well-known." (8 USPQ 2d at 1406). Similarly, the methods of transfecting cells, expressing protein, and measuring protein activity are well known, as evidenced by the Sun *et al.* publication and references cited therein.

6. *The relative skill of those in the art.* Those of skill in this art are highly skilled and would be competent at designing and performing, or directing the performance of, the procedures of factors (4) and (5) above. The Wands court found that the level of skill in the monoclonal antibody was high at the time the application was filed. Importantly, the court also found that *development of skill* in performing specific experiments relevant to the art did not preclude enablement. Specifically, the court stated that initial failures occurred as the inventors learned to fuse cells, and "[o]nce they became skilled in the art, they invariably obtained numerous hybridomas ..." that met the claim limitations. (8 USPQ 2d at 1406). By analogy, it would not defeat enablement for one of skill in the art of DNA transfection and expression to learn and become proficient in techniques for practicing the present invention.

7. *The predictability or unpredictability of the art.* One of skill, being acquainted with the methods described in the application, would predict that when PAR-1Bα is co-expressed in CHO cells with PAR-1 KN, the inhibitory effect of PAR-1 KN would be blocked. The person of skill, testing other polynucleotides as claimed, would predict that the outcome would reflect the ability of the test polynucleotide to encode a functional PAR-1 having kinase activity, and that this would be the only variable affecting the results. Those of skill in this art are acquainted with the need to run appropriate control experiments to rule out unrelated factors as affecting the results.

In Wands, the Court noted that the cell fusion technique was well known to those of ordinary skill in the art, and that there was no indication that the fusion step might be more difficult or unreliable for the antigen in question (HBsAg) than for other antigens. Finally, transfection of a CHO cell and measuring the presence of kinase activity is known, and the Examiner has provided no evidence that the transfection step would be "more difficult or unreliable" (8 USPQ2d at 1406) than for wild-type hPAR-1.

8. *The breadth of the claims.* Using materials and methods routinely available at the time of filing, one of skill can routinely identify or construct any nucleic aid molecule meeting the limitations of the claims, and test it for activity as described for the previous factors.

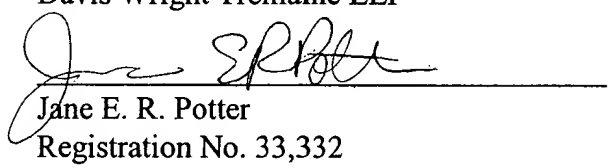
In view of the foregoing remarks, applicants submit that the Examiner has not met his burden of making a *prima facie* showing that undue experimentation is required in order to practice the invention as claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Espinosa *et al., Cytogenet Cell Genet.* 81:278-282 (1988) as evidenced by Espinosa *et al.,* Genbank Accession No. X97630, October 1998. Without acquiescing to the ground of rejection, applicants submit that the claims as amended are not subject to this ground of rejection.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
Tian-Qiang Sun et al.
Davis Wright Tremaine LLP



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EXPRESS MAIL NO. EL852691657US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Tian-Qiang Sun et al.
Application No.	: 09/919,585
Filed	: July 30, 2001
For	: ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES
Examiner	: Richard G. Hutson
Art Unit	: 1652
Docket No.	: 59516-147/PP-16093.002
Date	: August 6, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

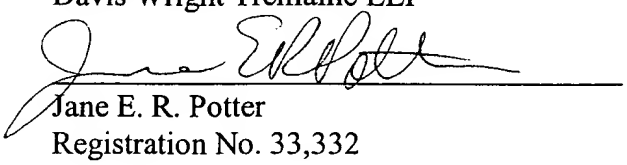
Commissioner for Patents:

In accordance with 37 C.F.R. §§ 1.56 and 1.97 through 1.98, applicants wish to make known to the Patent and Trademark Office the references set forth on the attached form PTO/SB/08 (copies of the cited references are enclosed). As to any reference supplied, applicants do not admit that it is "prior art" under 35 U.S.C. §§ 102 or 103, and specifically reserve the right to traverse or antedate any such reference, as by a showing under 37 C.F.R. § 1.131 or other method. Although the aforesaid references are made known to the Patent and Trademark Office in compliance with applicants' duty to disclose all information they are aware of which is believed relevant to the examination of the above-identified application, applicants believe that their invention is patentable.

Please acknowledge receipt of this Information Disclosure Statement and kindly make the cited references of record in the above-identified application.

A fee of $180 is submitted in accordance with 37 C.F.R. § 1.97(c). The Commissioner is authorized to charge any other fees which may be required, or credit any overpayment to Deposit Account No. 04-0258.

Respectfully submitted,
Tian-Qiang Sun et al.
Davis Wright Tremaine LLP



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PTO/SB/08B (05-03)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet	1	of	1		

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket Number	59516-147/PP-16093.002

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. [1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
		M. PEIFER ET AL., *Wnt Signaling in Oncogenesis and Embryogenesis – a Look Outside the Nucleus*, SCIENCE, 287:1606-1609, 2000	
		M. SHTUTMAN ET AL., *The Cyclin D1 Gene is a Target of the β-Catenin/LEF-1* Pathway, PROC. NATL. ACAD. SCI. U.S.A., 96:5522-5527, 1999	
		O. TETSU ET AL., *β-Catenin Regulates Expression of Cyclin D1 in Colon Carcinoma* Cells, NATURE, 398:422-426, 1999	
		J.D. BROWN ET AL., *Wnt Signaling:Why is Everything so Negative?*, CURR. OPIN. CELL BIOL., 10:182-187, 1998	
		T.C. HE ET AL., *Identification of c-MYC as a Target of the APC* Pathway, Science, 281:1509-1512, 1998	
		K.M. CADIGAN ET AL., *Wnt Signaling:A Common Theme in Animal* Development, GENES DEV., 11:3286-3305, 1997	
		J. KLINGENSMITH ET AL., *Conservation of Dishevelled Structure and Function Between Flies and Mice: Isolation and Characterization of Dv12*, MECH DEV., 58:15-26, 1996	
		K.W. KINZLER ET AL., *Lessons from Hereditary Colorectal* Cancer, CELL, 87:159-170, 1996	
		J. KLINGENSMITH ET AL., *The Drosophila Segment Polarity Gene Dishevelled Encodes a Novel Protein Required for Response to the Wingless Signal*, GENES DEV., 8:118-130, 1994	
		H. THEISEN ET AL., *Dishevelled is Required During Wingless Signaling to Establish Both Cell Polarity and Cell Identity*, DEVELOPMENT, 120:347-360, 1994	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents,** P.O. Box 1450, Alexandria, VA 22313-1450.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,585	07/30/2001	Tian-Qiang Sun	PP-16093.002	2590

7590 10/15/2003

Chiron Corporation
Intellectual Property R338
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETED on/by 10/17/03 /
Atty. CAL PA
File # PP16093.002
Due Date 4/15/03 Ext R55
Final Date 4/15/04 R50

ENTERED IN DWT
IP DOCKET
NOV 03 2003
By: M. Lanicek

PTO-90C (Rev. 10/03) 81

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER
	11

DATE MAILED:

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Commissioner for Patents

08/06/03

The reply filed on ~~12/9/2002~~ is not fully responsive to the prior Office Action because of the following omission(s) or matter(s): Applicants amendment of the claims is not correct as per 37 CFR 1.121 (c) part (1) "Amendment by rewriting, directions to cancel or add . Amendments to a claim must be made by rewriting such claim with all changes (e.g., additions, deletions, modifications) included. The rewriting of a claim (with the same number) will be construed as directing the cancellation of the previous version of that claim. A claim may also be canceled by an instruction." Specifically, applicants amendment of claim 1 has neglected to show changes of previous part (s) of claim 1. Applicants are reminded that amendments to claims made by rewriting must show all changes (i.e. additions, deletions modifications) included.

Since the above-mentioned reply appears to be bona fide, applicant is given ONE (1) MONTH or THIRTY (30) DAYS from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment. EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Primary Examiner
Art Unit 1652
October 14, 2003

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER

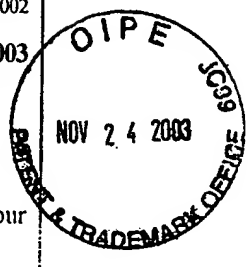
JEP:jeg

Docket No.: 59516-147/PP-16093.002

SENT: NOVEMBER 21, 2003

DUE: December 15, 2003

Date Stamp



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1. PTO/SB/21 Transmittal
2. PTO/SB/17 Fee Transmittal
3. PTO/SB/22 Extension of Time Request – 1m.
4. Amendment

In Re: Tian-Qiang Sung et al.; **for:** ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES; **Filed:** July 30, 2001; **as USAN:** 09/919,585

DAVIS WRIGHT TREMAINE LLP

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Docket No.: 59516-147/PP-16093.002

Date Stamp

SENT: NOVEMBER 21, 2003
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DAVIS WRIGHT TREMAINE LLP

LAWYERS

Davis Wright Tremaine LLP

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PTO/SB/21 (08-03)
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TRANSMITTAL FORM

(To be used for all correspondence after initial filing)

Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sung
Group Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket No.	59516-147/PP-16093.002

ENCLOSURES (*check all that apply*)

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [X] Amendment/Response
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [X] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement; Form PTO-1449
- [ ] Cited References
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts under 37 C.F.R. 1.52 or 1.53
- [ ] Response to Missing Parts/Incomplete Application
- [ ] Drawing(s)
- [ ] Request for Corrected Filing Receipt
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation, Change of Correspondence Address
- [ ] Declaration
- [ ] Statement under 37 CFR 3.73(b)
- [ ] Terminal Disclaimer
- [ ] Small Entity Statement
- [ ] Request for Refund
- [ ] CD(s), Number of CD(s)
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Return Receipt Postcard
- [ ] Additional Enclosure(s) *(please identify below)*:

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Individual Name	Jane E. R. Potter	27476
Signature	Jane E R Potter	
Date	November 21, 2003	

CERTIFICATE OF FACSIMILE TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date specified below.

Typed or printed name	Jessica Gaunt	
Signature	Jessica Gaunt	Date: November 21, 2003

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PTO/SB/17 (10-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 110

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sung
Examiner Name	Richard G. Hutson
Art Unit	1652
Attorney Docket No.	59516-147/PP-16093.002

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ None

☒ Deposit Account:

Deposit Account Number: 04-0258

Deposit Account Name: Davis Wright Tremaine LLP

The Commissioner is authorized to: *(check all that apply)*

☒ Charge fee(s) indicated below ☒ Credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, except for the filing fee

☒ Charge any deficiencies

to the above-identified deposit account.

FEE CALCULATION

1. **BASIC FILING FEE**

Large Entity Fee Code	Large Entity Fee($)	Small Entity Fee Code	Small Entity Fee($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	
				SUBTOTAL (1)	($) 0

2. **EXTRA CLAIM FEES**

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20** =		x		=	
Independent Claims		- 3** =		x		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** *Reissue independent claims over original patent*
1205	18	2205	9	** *Reissue claims in excess of 20 and over original patent*

SUBTOTAL (2) ($) 0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. **ADDITIONAL FEES**

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	110
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,330	2453	665	Petition to revive – unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Petitions related to provisional applications	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	
Other fee (specify) _____					

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($) 110

SUBMITTED BY				(Complete *(if applicable)*)	
Name (Print Type)	Jane E. R. Potter	*Registration No. (Attorney/Agent)*	33,332	Telephone	206-628-7650
Signature	Jane E R Potter			Date	November 21, 2003

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This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14.

PTO/SB/22 (05-03)
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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) 59516-147 / PP-16093.002

In re Application of Tian-Qiang Sung	
Application Number 09/919,585	Filed July 30, 2001
For ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES	
Art Unit 1652	Examiner Richard G. Hutson

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- ☒ One month (37 CFR 1.17(a)(1)) $ 110
- ☐ Two months (37 CFR 1.17(a)(2)) $ _____
- ☐ Three months (37 CFR 1.17(a)(3)) $ _____
- ☐ Four months (37 CFR 1.17(a)(4)) $ _____
- ☐ Five months (37 CFR 1.17(a)(5)) $ _____

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $_____.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 04-0258.

☒ The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account Number 04-0258.

I have enclosed a duplicate copy of this sheet.

I am the ☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☐ attorney or agent of record.

☒ attorney or agent under 37 CFR 1.34(a).
Registration number if acting under 37 CFR 1.34(a) 33,332.

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November 21, 2003
Date

Signature

206-628-7650
Telephone Number

Jane E. R. Potter
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ Total of 1 forms are submitted.

PATENT

I hereby certify that on the date specified below, this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

November 21, 2003
Date

Jessica Gaunt
Jessica Gaunt

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Tian-Qiang Sung et al.
Application No.	: 09/919,585
Filed	: July 30, 2001
For	: ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES
Examiner	: Richard G. Hutson
Art Unit	: 1652
Docket No.	: 59516-147/PP-16093.002
Date	: November 21, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

INTRODUCTORY COMMENTS

Commissioner for Patents:

In response to the Office Communication dated October 15, 2003, please extend the period of time for response one month to expire on December 15, 2003. Enclosed are a Petition for an Extension of Time and the required fee. Please amend the application as shown on the attached pages.

AMENDMENT TO THE CLAIMS

1. (Amended) An isolated nucleic acid molecule comprising a polynucleotide having a sequence selected from the group consisting of:

(a) ~~a sequence encoding amino acids from about 1 to about 744 of SEQ ID NO:3;~~

~~(b) a sequence encoding amino acids from about 2 to about 744 of SEQ ID NO:3;~~

~~(c)~~ a sequence encoding amino acids from ~~about~~ 1 to ~~about~~ 691 of SEQ ID NO:6;

~~(d)~~(b) a sequence encoding amino acids from ~~about~~ 2 to ~~about~~ 691 of SEQ ID NO:6;

~~(e) a sequence encoding amino acids from about 1 to about 724 of SEQ ID NO:9;~~

~~(f) a sequence encoding amino acids from about 2 to about 724 of SEQ ID NO:9;~~

~~(g) a sequence encoding amino acids from about 1 to about 795 of SEQ ID NO:12;~~

~~(h) a sequence encoding amino acids from about 2 to about 795 of SEQ ID NO:12;~~

~~(i)~~(c) complements of the sequences of (a)-~~(h)~~(b);

~~(j) a sequence having 50-2232 contiguous nucleotides from the coding region of SEQ ID NO:1;~~

~~(k)~~(d) a sequence having 50-2073 contiguous nucleotides from the coding region of SEQ ID NO:4;

~~(l) a sequence having 50-2172 contiguous nucleotides from the coding region of SEQ ID NO:7;~~

~~(m) a sequence having 50-2385 contiguous nucleotides from the coding region of SEQ ID NO:10;~~

~~(n)~~(e) sequences having at least ~~90%~~95% identity to the sequences of ~~(a) – (m)~~(b) – (d), wherein the polypeptide encoded by said sequence has kinase activity~~.~~;

~~(o)~~(f) sequences having 100-1500 contiguous nucleotides from the coding region of ~~SEQ ID NO:1,~~ SEQ ID NO:4~~, SEQ ID NO:7 or SEQ ID NO:10~~;

~~(p)~~(g) sequences having 500-1000 contiguous nucleotides from the coding region of ~~SEQ ID NO:1,~~ SEQ ID NO:4~~, SEQ ID NO:7 or SEQ ID NO:10~~;

~~(r)~~(h) sequences of (a) – ~~(h)~~(b)~~, except for at least one amino acid substitution in the encoded amino acid sequence; and~~ wherein said sequence encodes a polypeptide of SEQ ID NO:6 with at least one amino acid substitution, wherein said polypeptide has kinase activity;

~~(s)~~(i) sequences of (a) – ~~(h)~~(b), wherein said sequence encodes a polypeptide of SEQ ID NO:6 with ~~except for~~ a conversion of a conserved lysine to an alanine at an ATP binding site of ~~the encoded amino acid sequence~~ SEQ ID NO:6, wherein said polypeptide has kinase activity~~.~~;

(j) sequences of (f) – (g) wherein said sequence encodes a polypeptide having at least one amino acid substitution compared to the corresponding region of SEQ ID NO:6 encoded by said coding region; and

(k) sequences of (f) – (g) wherein said sequence encodes a polypeptide having a conversion of a conserved lysine to an alanine at an ATP binding site compared to the corresponding region of SEQ ID NO:6 encoded by said coding region.

2. (Original) A method of making a vector comprising inserting a nucleic acid molecule of claim 1 into said vector in operable linkage to a promoter.

3. (Original) A vector produced by the method of claim 2.

4. (Original) A method of making a host cell comprising transforming or transfecting a vector of claim 3 into a cell.

5. (Original) A host cell produced by the method of claim 4.

6. (Original) A method of making a polypeptide, comprising culturing the host cell of claim 5 under conditions such that said polypeptide is expressed and recovering said polypeptide.

7-25. (Withdrawn)

REMARKS

Applicants submit this response to the Office Action dated May 6, 2003 and the Office Communication dated October 15, 2003. As a result of a restriction requirement dated October 1, 2002, the invention has been restricted into six claim groups (I-VI), and further into four sequence groups (A-D), whereby election of one of group I-VI, and one of group A-D was required. Applicants elected group I, directed to nucleic acid vectors, host cells comprising same and methods of expression of the nucleic acid, and group (B) comprising nucleotide sequence SEQ ID NO:4 and amino acid sequence SEQ ID NO:6. As a result, claims 1-6 are pending and claims 7-25 are withdrawn from consideration. Claim 1 is amended to recite the elected sequences, and further amendments are discussed below. The recitation of "95% identity" in claim 1 is supported at least at page 60, lines 7-9 of the specification. No new matter is added.

An Information Disclosure Statement is filed herewith to confirm that the patents and publications intended to be disclosed for the record, and which are cited in the specification, are made of record.

Claims 1-6 are objected to for reciting nonelected subject matter. This has been addressed by amending independent claim 1, from which claims 2-6 depend.

Claims 1-6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Without acquiescing to the ground of rejection, applicants submit that claim 1 as amended is not subject to the specific grounds of objection ("about" language, and "ATP binding site").

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification so as to reasonably convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention. Without acquiescing to the ground of rejection, applicants have amended claim 1, from which claims 2-6 depend. The Examiner recommended adding functional language to the rejected claims (Office Action, page 5, lines 8-9), and the amended claims address this issue. The kinase activity of the polypeptide expressed by the claimed nucleic acid molecule is disclosed in the specification at, for example, page 245, first paragraph and page 247, lines 10-12. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph (enablement). The Examiner states that the specification is enabling for a nucleic acid molecule comprising a

polynucleotide sequence encoding SEQ ID NO:6. However, the specification allegedly is not enabling for any nucleic acid molecule at least 90% identical to a sequence encoding SEQ ID NO:6; a sequence that is 50, 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO:4; or any sequence except for at least one amino acid substitution in the encoded amino acid sequence. The Examiner cited the Wands factors (*In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988)).

A specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a *prima facie* case of lack of enablement. See, In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976); In re Marzocchi, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). To make a *prima facie* case of lack of enablement, the PTO must come forward with reasons, supported by the record as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). The mere fact that some experimentation is necessary does not negate enablement as long as undue experimentation is not required. See M.P.E.P. § 608.01(p).

The burden is on the PTO to establish that experimentation would be undue, Angstadt, 190 U.S.P.Q. at 219, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experimentation. In re Wands, 8 U.S.P.Q.2d 1400, 1404 (C.A.F.C. 1988). Applicants submit that the amount of experimentation that may be required to practice the present invention does not rise to the level of being undue experimentation, as defined by the Court in Wands.

An important aspect of the Court's decision in Wands is its finding that the nature of the technology pertinent to the Wands invention (monoclonal antibody production) permitted a broad definition of the term "experiment." The Court found that an "experiment" in the monoclonal antibody art consisted of the entire attempt to make a monoclonal antibody against a particular antigen. As described by the Court, the process entailed, "immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 8 U.S.P.Q.2d at 1407. Thus, Wands supports the conclusion that, in a complex

field such as monoclonal antibody production, the entire attempt to achieve the desired result, from beginning to end, constitutes one experiment.

According to the Court, repetition of this whole experiment more than once does not constitute undue experimentation. As the Court indicated, practitioners in the art would be prepared to screen negative hybridomas in order to find a hybridoma making the desired antibody. 8 U.S.P.Q.2d at 1406. Thus, the fact that some aspects of the experiment as a whole may yield negative results does not mandate a finding that the amount of experimentation to achieve a positive result is undue.

Applying this information to the eight Wands factors, one of skill in the art would conclude that undue experimentation would not be required to practice the claimed invention.

1. *Quantity of experimentation necessary.* Applicants submit that one of ordinary skill in the art can construct a hybridization probe based on the disclosed polynucleotide, SEQ ID NO:6, and use the probe to locate and obtain hybridizing DNA. The polypeptide encoded by the hybridizing DNA would be tested for PAR-1Bα activity (as claimed, kinase activity), and the polynucleotide would be evaluated on the basis of the limitations of the claimed identity with the amino acid sequence of SEQ ID NO:4. If the results of these routine procedures were positive, the polynucleotide sequence would fall within the scope of the claims. Such tests would not constitute "undue" experimentation within the scope of Wands. To determine if a polynucleotide falls within the scope of the claims, the only experimentation required is the performance of transfection and assay procedures. These procedures are routine and would not have to be done repeatedly before a clear result was obtained. Because the inventors and the art provide means for the objective measurement of a polynucleotide falling within the claim scope, this factor is met, for example, by the ability of the polynucleotide to encode a protein capable of blocking the inhibitory activity of mutant Kinase-negative PAR-1 (KN PAR-1). This is described in the specification at pages 246-247.

The Wands court found that practitioners in the art are prepared to screen negative hybridomas to find one that made the desired antibody. (8 USPQ2d at 1406.) The court further stated that an "experiment" was not simply the screening of a single hybridoma, but instead was the entire attempt to make a monoclonal antibody against a particular antigen. This process included immunizing animals, fusing lymphocytes from the immunized animals to make

hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas. (8 USPQ2d at 1406).

By analogy, a single experiment in the present art could include obtaining or constructing a polynucleotide, transfecting it into CHO cells that co-express wild-type PAR-1, and determining if Dvl is phosphorylated. Encountering negative results would not mean that undue experimentation is involved, according to Wands.

2. *Amount of direction or guidance provided.* Like the production of monoclonal antibodies, the identification or production of DNA encoding a polypeptide having PAR-1B α activity and falling within the scope of the claims may require some experimentation, but if viewed in the light of Wands, this experimentation is not undue. The present applicants provide extensive guidance to allow one of ordinary skill in the art to obtain DNA that is within the scope of the claims. The Examiner stated that "it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims..." (Page 7, first full paragraph.) Applicants, first, request that the Examiner provide support for this statement about what is and is not routine in this art. Second, the claims do not require a practitioner in this art to "screen for multiple substitutions or multiple modifications." Instead, the screening would entail testing one or more polypeptides for activity as described in the specification, to determine if a given polynucleotide encodes a polypeptide within the scope of the claims. The specification provides clear directions for performing the procedures, and provides cites to published scientific articles for details not mentioned in the specification. Similarly, the Wands court found that the starting material was available to the public (as is the material used in the present application) and the patent application at issue in Wands provided a detailed description of the methods, which included use of a commercially available kit. (8 USPQ 2d at 1404, 1405). The cell lines used in applicants' methods are commercially available, and the application describes the methods, at pages 245-247.

3. *Presence or absence of working examples.* The specification describes transfection of CHO cells using a claimed polynucleotide of the invention, specifically PAR-1B α. (Page 247, lines 10-11.) The co-expression experiment provides an example that is applicable to other claimed polynucleotides (test polynucleotides), which would be co-expressed

in the CHO cells along with the mutant (PAR-1 KN) construct. The blocking of inhibitory effects of PAR-1 KN would signal that the test polynucleotide is within the scope of the claims.

These experiments show that it is routine to detect the effect of PAR-1 inhibition. This can be accomplished by transfecting HT1080 cells with an antisense oligonucleotide, lysing the cells after a period of incubation, and analyzing (a) PAR-1 protein content using antibodies, and (b) activity of a reporter gene, specifically a LEF1 reporter. These experiments provide an objective way of measuring PAR-1 activity. The methods are disclosed in the Sun *et al.* publication. These methods are also disclosed in the present patent application at page 247-248, Example 6.

Example 5 of the application, at pages 246-247, describes experiments in which cDNAs for PAR-1 were transfected into Chinese hamster ovary (CHO) cells. In one set of experiments, cDNAs encoding mutant forms of PAR-1, which did not have kinase activity, were transfected into CHO cells. In the absence of the kinase activity, the target of PAR-1 phosphorylation, Dishevelled (Dvl), is not phosphorylated. This result is detected as a reduced amount of a retarded Dvl band. Importantly for the purposes of this invention, if wild-type PAR-1 (capable of phosphorylating Dsl) is co-expressed with the mutant forms of PAR-1 in the CHO cells, the inhibitory activity of the mutant PAR-1 is blocked. This provides a method for determining if a polynucleotide sequence with a given percent homology to SEQ ID NO:6 is capable of functioning as a wild-type PAR-1 sequence, namely, able to encode functional PAR-1 protein. Such experimentation is routine, as it employs known methods and known materials, and needs only the addition of a test polynucleotide to measure objectively whether the polynucleotide falls within the scope of the claims.

4. *Nature of the invention.* The inventors have, for the first time, identified and cloned a human homologue of the *Drosophila* gene referred to as PAR-1. Three human homologues were identified and cloned, and one, the PAR-1Bα form, is under examination in this application. As discussed in a related publication by the inventors, Sun, Tian-Qiang *et al.*, "PAR-1 is a Disheveled-associated kinase and a positive regulator of Wnt signaling," *Nature Cell Biology* 3:628-636, 2001, PAR-1 plays a role in a pathway referred to as the Wnt pathway. Through a series of receptor interactions, Wnt enhances the ability of a protein to antagonize the activity of glycogen synthase kinase 3β. The effect of this pathway, and the associated

interactions of the components, is to stabilize the cytosolic protein β-catenin. β-catenin in turn moves to the nucleus, where it combines with a transcription factor to regulate expression of genes. In humans, abnormalities in regulation of the Wnt pathway can cause cancer, as described below. PAR-1 has been shown by the inventors to modulate this Wnt-β-catenin pathway. Thus, it is an important protein from the perspective of its role in normal cell function, and because the Wnt pathway is implicated in cancer, proteins that play a role in this pathway are also implicated in cancer. Functionally, PAR-1 is a serine-threonine kinase.

The inventors designed and performed experiments to determine how cells would react to inhibition of PAR-1. HT1080 cells were chosen because oligonucleotides such as antisense RNA can be delivered to these cells with relative ease, and because HT1080 has a robust transcriptional response to Wnt, allowing the investigator to detect changes in gene expression resulting from disruption of this pathway. (Sun *et al.*, page 632, left column, lines 10-17.) Antisense oligonucleotides capable of specifically binding to PAR-1 reduced PAR-1 messenger RNA (mRNA) by 75-90%, and also reduced PAR-1 protein levels. The inhibition was accompanied by a reduction in Wnt-induced reporter activity. (Sun *et al.*, page 632, left column, lines 17-20). These results showed that (a) it is possible to connect an inhibition of PAR-1 with processes associated with PAR-1 activity, and (b) it is possible to *selectively* inhibit PAR-1 mRNA levels and protein levels. This selective inhibition is achieved using antisense oligonucleotides that specifically recognize and hybridize with PAR-1 sequences of the invention.

The invention relates to human polynucleotides. Methods of synthesizing, isolating, mutating, manipulating, transfecting, and expressing polynucleotides are the basis of the biotechnology industry. The nature of the invention is such that it is well-known to those of ordinary skill in the art.

5. *The state of the prior art.* The prior art provides the methods and materials needed to apply the methods of factor (4) above to this group of polynucleotides, specifically hPAR-1 polynucleotides. The Wands court found that "all the methods needed to practice the invention were well-known." (8 USPQ 2d at 1406). Similarly, the methods of transfecting cells, expressing protein, and measuring protein activity are well known, as evidenced by the Sun *et al.* publication and references cited therein.

6. *The relative skill of those in the art.* Those of skill in this art are highly skilled and would be competent at designing and performing, or directing the performance of, the procedures of factors (4) and (5) above. The Wands court found that the level of skill in the monoclonal antibody was high at the time the application was filed. Importantly, the court also found that *development of skill* in performing specific experiments relevant to the art did not preclude enablement. Specifically, the court stated that initial failures occurred as the inventors learned to fuse cells, and "[o]nce they became skilled in the art, they invariably obtained numerous hybridomas ..." that met the claim limitations. (8 USPQ 2d at 1406). By analogy, it would not defeat enablement for one of skill in the art of DNA transfection and expression to learn and become proficient in techniques for practicing the present invention.

7. *The predictability or unpredictability of the art.* One of skill, being acquainted with the methods described in the application, would predict that when PAR-1Bα is co-expressed in CHO cells with PAR-1 KN, the inhibitory effect of PAR-1 KN would be blocked. The person of skill, testing other polynucleotides as claimed, would predict that the outcome would reflect the ability of the test polynucleotide to encode a functional PAR-1 having kinase activity, and that this would be the only variable affecting the results. Those of skill in this art are acquainted with the need to run appropriate control experiments to rule out unrelated factors as affecting the results.

In Wands, the Court noted that the cell fusion technique was well known to those of ordinary skill in the art, and that there was no indication that the fusion step might be more difficult or unreliable for the antigen in question (HBsAg) than for other antigens. Finally, transfection of a CHO cell and measuring the presence of kinase activity is known, and the Examiner has provided no evidence that the transfection step would be "more difficult or unreliable" (8 USPQ2d at 1406) than for wild-type hPAR-1.

8. *The breadth of the claims.* Using materials and methods routinely available at the time of filing, one of skill can routinely identify or construct any nucleic aid molecule meeting the limitations of the claims, and test it for activity as described for the previous factors.

In view of the foregoing remarks, applicants submit that the Examiner has not met his burden of making a *prima facie* showing that undue experimentation is required in order to

practice the invention as claimed. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Espinosa *et al., Cytogenet Cell Genet.* 81:278-282 (1988) as evidenced by Espinosa *et al.*, Genbank Accession No. X97630, October 1998. Without acquiescing to the ground of rejection, applicants submit that the claims as amended are not subject to this ground of rejection.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
Tian-Qiang Sung et al.
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By _____
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7590 02/20/2004

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

DOCKETED on/by 2/27/04 ow
Atty. CAL PA
File # PP16093.002
Due Date 4/20/04 Ext RF4
Final Date 8/20/04 RF8, NA8

Office Action Summary	Application No.	Applicant(s)	
	09/919,585	SUN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *7-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendment of claim 1, Paper of 11/24/2003, is acknowledged. Claims 1-25 are at issue and are present for examination. Applicants' arguments filed on 11/24/2003, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 7-25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

Applicants filing of information disclosure, filed 8/6/2003, is acknowledged. Those references considered have been initialed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-6 dependent on) is indefinite in that it is vague and confusing in the recitation in part (s) "...except for a conversion of a conserved lysine to an alanine at an ATP binding site of the encoded amino acid sequence" . It is vague and unclear what

applicants consider to be an ATP binding site of the sequences of (c) and (d) (i.e. SEQ ID NO: 6).

In response to this previous rejection applicants have amended claims 1 and submit that without acquiescing to the ground of rejection, applicants amendment is not subject to the specific grounds of objection ("about" language and "ATP binding site"). Applicants comments and amendment are acknowledged, however the rejection is maintained, in light of applicants have not explained why the ATP binding site of the sequences of SEQ ID NO: 6 is not unclear.

Newly amended claim 1 (2-6 dependent on) is indefinite in that part (h) and (i) each recite "sequences of (a)-(b), and then go on to attempt to change the referred to sequence. This is unclear and confusing since each of the referred to sequences of (a) and (b) are drawn to sequences (i.e. that of SEQ ID NO: 6) that if changed would no longer be SEQ ID NO: 6. Thus it is unclear what applicants intent is in each of these parts of the claim. It is further noted and as an example, that part (h) recites "sequences of (a)-(b) wherein said sequence encodes a polypeptide of SEQ ID NO: 6 with at least one amino acid substitution, wherein said polypeptide has kinase activity". Such a claim limitation effectively reads on **any** and **all** kinases with the exception of SEQ ID NO: 6.

Newly amended claim 1 (2-6 dependent on) is indefinite in that part (j) and (k) are each indefinite in that they are unclear and confusing as they do not appear to further limit the genus of sequences from which they depend.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1-6. In response to the rejection applicants have amended claim 1 and traverse this rejection as it applies to the newly rejected claims.

Applicants submit that the examiner recommended adding functional language to the rejected claims and that the amended claims address this issue.

Applicants amendment and argument is not found persuasive because while applicants have added "functional language" to specific subsections of the claim such as part (e), it remains that this added "functional language" merely describes but a small portion of the claimed molecules. Further even if applicants were to amend the claims such that the entire genus claimed had the discussed functional limitation, it remains that certain portions of the claim still require additional structural characterization to adequately describe them. As stated in the previous office action, applicant is advised to in **addition to more structural detail**, adding functional language to the rejected claims such that an adequate structure to function/activity relationship of the claimed genus is described.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising a polynucleotide sequence encoding SEQ ID NO: 6, does not reasonably provide enablement for any nucleic acid molecule comprising a polynucleotide sequence at least 95% identical to a sequence encoding SEQ ID NO: 6, or sequence that is a mere 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, or any sequence except for at least one amino acid substitution in the encoded amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-6. In response to the rejection applicants have amended claim 1 and traverse this rejection as it applies to the newly rejected claims.

Applicants submit that the amount of experimentation that may be required to practice the present invention does not rise to the level of being undue experimentation as defined by the court in Wands.

Applicants submit that applying the eight Wands factors, one of skill in the art would conclude that undue experimentation would not be required to practice the

claimed invention. In so doing so applicants submit arguments under headings of each of the wands factors. Applicants submit that the quantity of experimentation necessary: is not undue as one can use a hybridization probe to locate and obtain hybridizing DNA, which can be tested for activity. Applicants submit that the amount of direction or guidance presented by the specification is sufficient, and that applicants describe examples of a transfection/transformation of a claimed polynucleotide. Applicants submit that the nature of the invention is such that applicants have cloned a human homologue of the PAR-1 gene and that the prior art provides methods and materials and the level of skill in the art is high. Finally applicants submit that the art is predictable and the breadth of the claim(s) routinely identified and/or constructed.

Applicants argument is not found persuasive for the reasons previously stated. The claims rejected under this section of U.S.C. 112, first paragraph, place minor structural limits on the claimed nucleic acid molecules such that adequate guidance is disclosed with respect to how to make and use the majority of the scope of the claimed genus. Applicants are reminded that the claimed genus of polynucleotides encompasses any polynucleotide which meets the minor structural limitations of the claims (i.e. see parts d, f. g and h), and most of the encompassed molecules have no structural limitation.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any nucleic acid molecule comprising a polynucleotide sequence that is a mere 100 or 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, because the specification does not establish: (A) regions of the

protein and thus polynucleotide structure which may be modified without effecting its activity; (B) the general tolerance of serine/threonine protein kinases and their encoding polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a serine/threonine protein kinases with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain a function/activity of the claimed polynucleotides or their encoded polypeptides and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable it would require undue experimentation for one skilled in the art to **arrive at and use** the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any polynucleotide encoding SEQ ID NO: 6. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Espinosa et al., (Human serine/threonine protein kinase EMK1: genomic structure and cDNA cloning of isoforms produced by alternative splicing, Cytogenet. Cell Genet., Vol 81, No 3/4, pages 278-282, 1998, Ref V, enclosed 892) as evidenced by Espinosa et al. (Genbank Accession Number X97630, October 1998).

The rejection was stated in the previous office action and repeated below for applicants convenience.

Espinosa et al. teach isolation and cloning of a polynucleotide that encodes two isoforms of the human serine/threonine protein kinase EMK1 and Espinosa et al. teach vectors and host cells comprising said polynucleotide and methods of making said vectors and host cells. The polynucleotide isolated, cloned and disclosed by Espinosa et al. has a best local similarity score of greater then 92% when compared to the sequence of SEQ ID NO: 4 and the taught nucleic acid comprises polynucleotide sequences of at least 500 contiguous nucleotides of the coding region of SEQ ID NO: 4, as evidenced by Espinosa et al. (Genbank Accession Number X97630, October 1998).

Therefore, Espinosa et al. anticipates claims 1-6.

In response to this rejectin applicants have amended claim 1 and submit that the claims as amended are not subject to the ground of this rejection. Applicants comments are noted, however, the rejection remains. Applicants attention is drawn to amended claim 1 parts (d), (f), (g) (h), (j) and (k), (See above 112 second paragraph rejection also) all of which remain anticipated by Espinosa et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
2/13/2004

PTO/SB/08B (05-03)
Approved for use through 04/30/2003. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet | | of | 1

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket Number	59516-147/PP-16093.002

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
RH		M. PEIFER ET AL., *Wnt Signaling in Oncogenesis and Embryogenesis – a Look Outside the Nucleus*, SCIENCE, 287:1606-1609, 2000	
		M. SHTUTMAN ET AL., *The Cyclin D1 Gene is a Target of the β-Catenin/LEF-1* Pathway, PROC. NATL. ACAD. SCI. U.S.A., 96:5522-5527, 1999	
		O. TETSU ET AL., *β-Catenin Regulates Expression of Cyclin D1 in Colon Carcinoma* Cells, NATURE, 398:422-426, 1999	
		J.D. BROWN ET AL., *Wnt Signaling:Why is Everything so Negative?*, CURR. OPIN. CELL BIOL., 10:182-187, 1998	
		T.C. HE ET AL., *Identification of c-MYC as a Target of the APC* Pathway, Science, 281:1509-1512, 1998	
		K.M. CADIGAN ET AL., *Wnt Signaling:A Common Theme in Animal* Development, GENES DEV., 11:3286-3305, 1997	
		J. KLINGENSMITH ET AL., *Conservation of Dishevelled Structure and Function Between Flies and Mice: Isolation and Characterization of Dv12*, MECH DEV., 58:15-26, 1996	
		K.W. KINZLER ET AL., *Lessons from Hereditary Colorectal* Cancer, CELL, 87:159-170, 1996	
		J. KLINGENSMITH ET AL., *The Drosophila Segment Polarity Gene Dishevelled Encodes a Novel Protein Required for Response to the Wingless Signal*, GENES DEV., 8:118-130, 1994	
RH		H. THEISEN ET AL., *Dishevelled is Required During Wingless Signaling to Establish Both Cell Polarity and Cell Identity*, DEVELOPMENT, 120:347-360, 1994	

Examiner Signature		Date Considered	2/13/04

*EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant.

[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.

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Docket No.: 59516-147/PP-16093.002

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DUE: August 20, 2004

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In Re: Tian-Qiang Sun et al.; **for:** ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES; **Filed:** July 30, 2001; **as USAN:** 09/919,585

DAVIS WRIGHT TREMAINE LLP

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Docket No.: 59516-147/PP-16093.002

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TRANSMITTAL FORM

(To be used for all correspondence after initial filing)

Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Group Art Unit	1652
Examiner Name	Richard G. Hutson
Attorney Docket No.	59516-147/PP-16093.002

ENCLOSURES (*check all that apply*)

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [X] Amendment/Response
  - [X] After Final
  - [ ] Affidavits/declaration(s)
- [X] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement; Form PTO-1449
- [ ] Cited References
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts under 37 C.F.R. 1.52 or 1.53
- [ ] Response to Missing Parts/Incomplete Application
- [ ] Drawing(s)
- [ ] Request for Corrected Filing Receipt
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation, Change of Correspondence Address
- [ ] Declaration
- [ ] Statement under 37 CFR 3.73(b)
- [ ] Terminal Disclaimer
- [ ] Small Entity Statement
- [ ] Request for Refund
- [ ] CD(s), Number of CD(s)
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [X] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Return Receipt Postcard
- [ ] Additional Enclosure(s) *(please identify below)*:

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Individual Name	Jane E. R. Potter, Registration No. 33,332	27476
Signature		
Date	August 19, 2004	

CERTIFICATE OF FACSIMILE TRANSMISSION/MAILING

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FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 1280

Complete if Known	
Application Number	09/919,585
Filing Date	July 30, 2001
First Named Inventor	Tian-Qiang Sun
Examiner Name	Richard G. Hutson
Art Unit	1652
Attorney Docket No.	59516-147/PP-16093.002

METHOD OF PAYMENT *(check all that apply)*

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee($)	Small Entity Fee Code	Small Entity Fee($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) 0

2. EXTRA CLAIM FEES

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20** =		x		=	
Independent Claims		- 3** =		x		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** *Reissue independent claims over original patent*
1205	18	2205	9	** *Reissue claims in excess of 20 and over original patent*

SUBTOTAL (2) ($) 0

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FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	950
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	330
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,330	2453	665	Petition to revive – unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Petitions related to provisional applications	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

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SUBMITTED BY (Complete *(if applicable)*)

Name (Print Type)	Jane E. R. Potter	*Registration No. (Attorney/Agent)*	33,332	Telephone	206-628-7650
Signature				Date	August 19, 2004

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RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE – EXAMINING GROUP 1600

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Tian-Qiang Sun et al.
Application No.	: 09/919,585
Filed	: July 30, 2001
For	: ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES
Examiner	: Richard G. Hutson
Art Unit	: 1652
Docket No.	: 59516-147/PP-16093.002
Date	: August 19, 2004

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RESPONSE UNDER 37 C.F.R. § 1.116

INTRODUCTORY COMMENTS

Commissioner for Patents:

In response to the Office Action dated February 20, 2004, please extend the period of time for response three months to expire on August 20, 2004. Enclosed are a Petition for an Extension of Time and the required fee. Please amend the application as shown on the attached pages.

AMENDMENT TO THE CLAIMS

1. (Currently Amended) An isolated nucleic acid molecule comprising a polynucleotide having a sequence selected from the group consisting of:

(a) a sequence encoding amino acids from 1 to 691 of SEQ ID NO:6;

(b) a sequence encoding amino acids from 2 to 691 of SEQ ID NO:6; and

(c) complements of the sequences of (a)-(b);

~~(d) a sequence having 50-2073 contiguous nucleotides from the coding region of SEQ ID NO:4;~~

~~(e) sequences having at least 95% identity to the sequences of (b) (d), wherein the polypeptide encoded by said sequence has kinase activity;~~

~~(f) sequences having 100-1500 contiguous nucleotides from the coding region of SEQ ID NO:4;~~

~~(g) sequences having 500-1000 contiguous nucleotides from the coding region of SEQ ID NO:4;~~

~~(h) sequences of (a) (b), wherein said sequence encodes a polypeptide of SEQ ID NO:6 with at least one amino acid substitution, wherein said polypeptide has kinase activity;~~

~~(i) sequences of (a) (b), wherein said sequence encodes a polypeptide of SEQ ID NO:6 with a conversion of a conserved lysine to an alanine at an ATP binding site of SEQ ID NO:6, wherein said polypeptide has kinase activity;~~

~~(j) sequences of (f) (g) wherein said sequence encodes a polypeptide having at least one amino acid substitution compared to the corresponding region of SEQ ID NO:6 encoded by said coding region; and~~

~~(k) sequences of (f) (g) wherein said sequence encodes a polypeptide having a conversion of a conserved lysine to an alanine at an ATP binding site compared to the corresponding region of SEQ ID NO:6 encoded by said coding region.~~

2. (Original) A method of making a vector comprising inserting a nucleic acid molecule of claim 1 into said vector in operable linkage to a promoter.

3. (Original) A vector produced by the method of claim 2.

4. (Original) A method of making a host cell comprising transforming or transfecting a vector of claim 3 into a cell.

5. (Original) A host cell produced by the method of claim 4.

6. (Original) A method of making a polypeptide, comprising culturing the host cell of claim 5 under conditions such that said polypeptide is expressed and recovering said polypeptide.

7. (Withdrawn) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences having at least 95% identity to an amino acid sequence of:

(i) amino acids from about 1 to about 744 of SEQ ID NO:3,

(ii) amino acids from about 2 to about 744 of SEQ ID NO:3,

(iii) amino acids from about 1 to about 691 of SEQ ID NO:6,

(iv) amino acids from about 2 to about 691 of SEQ ID NO:6,

(v) amino acids from about 1 to about 724 of SEQ ID NO:9,

(vi) amino acids from about 2 to about 724 of SEQ ID NO:9,

(vii) amino acids from about 1 to about 795 of SEQ ID NO:12, or

(viii) amino acids from about 2 to about 795 of SEQ ID NO:12;

(b) sequences having, expect for at least one amino acid substitution, an amino acid sequence of: (i) – (viii);

(c) sequences having, expect for at least one amino acid substitution, an amino acid sequence of: (i) – (viii); and

(d) sequences having, expect for a conversion of a conserved lysine to an alanine at the ATP binding site of said polypeptide, an amino acid sequence of: (i) – (viii).

8. (Withdrawn) An epitope-bearing portion of a polypeptide selected from the group consisting of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:9 and SEQ ID NO:12.

9. (Withdrawn) The epitope-bearing portion of claim 8, which comprises about 5 to about 50 contiguous amino acids.

10. (Withdrawn) An isolated antibody that binds to the polypeptide of claim 7.

11. (Withdrawn) A complex comprising a polypeptide of claim 7 and a Dishevelled protein.

12. (Withdrawn) A complex comprising a fragment of a polypeptide of claim 7 and a Dishevelled protein.

13. (Withdrawn) A method of identifying an inhibitor or enhancer of PAR-1 phosphorylation activity, comprising:

(a) contacting a cell transfected with at least an expression vector encoding Wnt with a candidate inhibitor or enhancer; and

(b) detecting an increase or decrease in Dsh phosphorylation,

wherein a decrease in Dsh phosphorylation indicates the presence of an inhibitor and an increase in Dsh phosphorylation indicates the presence of an enhancer.

14. (Withdrawn) An isolated PAR-1 modulator selected from the group consisting of an antisense oligonucleotide, a ribozyme, a protein, a polypeptide, and a small molecule.

15. (Withdrawn) The isolated PAR-1 modulator of claim 14, wherein said PAR-1 modulator is an antisense molecule or the complement thereof.

16. (Withdrawn) The isolated PAR-1 modulator of claim 15, wherein said antisense molecule or the complement thereof has at least 15 consecutive nucleic acids of the sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:9 or SEQ ID NO:12 or which hybridizes under high stringency conditions to said at least 15 consecutive nucleic acids of the sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:9 or SEQ ID NO:12.

17. (Withdrawn) The isolated PAR-1 modulator of claim 15, wherein said antisense molecule is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:15 and SEQ ID NO:17.

18. (Withdrawn) The isolated PAR-1 modulator of claim 14, wherein said PAR-1 modulator is selected from the group consisting of an antibody and an antibody fragment.

19. (Withdrawn) The isolated PAR-1 modulator of claim 14, wherein said polypeptide has an amino sequence with at least 95% identity to the amino acid sequence provided in SEQ ID NO:22.

20. (Withdrawn) A composition, comprising a therapeutically effective amount of a PAR-1 modulator of claim 14 in a pharmaceutically acceptable carrier.

21. (Withdrawn) A method of treating a mammal with a disease or disorder associated with a PAR-1 polypeptide, comprising administering to the mammal a composition including a therapeutically effective amount of a PAR-1 modulator of claim 14.

22. (Withdrawn) The method of claim 23, wherein said PAR-1 modulator is an antisense molecule is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:15 and SEQ ID NO:17.

23. (Withdrawn) The method of claim 21, wherein said PAR-1 modulator is a polypeptide that has an amino sequence with at least 95% identity to the amino acid sequence provided in SEQ ID NO:22.

24. (Withdrawn) The method of claim 21, wherein said PAR-1 modulator is selected from the group consisting of an antibody and an antibody fragment.

25. (Withdrawn) The method of claim 21, wherein said PAR-1 modulator is administered *ex vivo* to said mammalian cell.

REMARKS

Applicants submit these remarks in response to the Office Action dated February 20, 2004. Claims 1-6 are pending, and claims 7-25 have been withdrawn from consideration following a restriction requirement. Claim 1 is amended as discussed below and no new matter is added. Applicants thank the Examiner for acknowledging receipt and consideration of the Information Disclosure Statement filed on August 6, 2003.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, in view of language regarding conversion of a conserved lysine to an alanine at an ATP binding site. The Examiner asserts that the "ATP binding site" language is unclear. Claim 1 allegedly is unclear in the recitations in part (h) and (i) in reference to sequences of (a) – (b), and parts (j) and (k) of claim 1 also allegedly are unclear. Applicants submit that claim 1 as amended (and claims 2-6 depending from claim 1) are no longer subject to this ground of rejection, withdrawal of which is respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner has maintained this ground of rejection, and states that further structural detail would be required to satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Without acquiescing to this ground of rejection, applicants submit that claim 1 as amended is not subject to this ground of rejection, nor are dependent claims 2-6. Withdrawal of this rejection is respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement in the specification. The Examiner states that the specification is enabling for a nucleic acid molecule comprising a sequence encoding SEQ ID NO:6. Applicants submit that claim 1 as amended (and claims 2-6 depending from claim 1) are no longer subject to this ground of rejection, withdrawal of which is respectfully requested.

Claims 1-6 are rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Espinosa et al., Cytogenet. Cell Genet. 81:278-282, 1998) as evidence by Espinosa et al., Genbank Accession No. X97630, October 1998. Applicants submit that the claims as amended herein are not subject to this ground of rejection, withdrawal of which is respectfully requested.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
Tian-Qiang Sun et al.
DAVIS WRIGHT TREMAINE LLP

By _____
Jane E. R. Potter
Registration No. 33,332

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1501 Fourth Avenue
Seattle, WA 98101-1688
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EXPRESS MAIL NO. EV398877402US

PTO/SB/22 (05-03)
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) 59516-147 PP-16093.002

In re Application of Tian-Qiang Sun et al.	
Application Number 09/919,585	Filed July 30, 2001
For ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES	
Art Unit 1652	Examiner Richard G. Hutson

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- ☐ One month (37 CFR 1.17(a)(1)) $ _____
- ☐ Two months (37 CFR 1.17(a)(2)) $ _____
- ☒ Three months (37 CFR 1.17(a)(3)) $ 950
- ☐ Four months (37 CFR 1.17(a)(4)) $ _____
- ☐ Five months (37 CFR 1.17(a)(5)) $ _____

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: $_____.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 04-0258.

☒ The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account Number 04-0258.

I have enclosed a duplicate copy of this sheet.

I am the
- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71 Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).
- ☐ attorney or agent of record.
- ☒ attorney or agent under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a) 33,332.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

August 19, 2004
Date

Signature

206-628-7650
Telephone Number

Jane E. R. Potter
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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PTO/SB/31 (05-03)
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

NOTICE OF APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Docket Number
59516-147/PP-16093.002

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

Signature SENT VIA EXPRESS MAIL

Typed or printed name

In re Application of

Tian-Qiang Sun et al.

Application Number	Filed
09/919,585	July 30, 2001

For ISOLATION OF DROSOPHILA AND HUMAN POLYNUCLEOTIDES ENCODING PAR-1 KINASE, POLYPEPTIDES ENCODED BY THE POLYNUCLEOTIDES AND METHODS UTILIZING THE POLYNUCLEOTIDES AND POLYPEPTIDES

Group Art Unit	Examiner
1652	Richard G. Hutson

Applicant hereby appeals to the Board of Patent Appeals and Interferences from the last decision of the examiner.

The fee for this Notice of Appeal is (37 CFR 1.17(b)) $330.

☐ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by half, and the resulting fee is: $____.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Commissioner has already been authorized to charge fees in this application to a Deposit Account. I have enclosed a duplicate copy of this sheet.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 04-0258. I have enclosed a duplicate copy of this sheet.

☒ A petition for an extension of time under 37 CFR 1.136(a) (PTO/SB/22) is enclosed.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71.
Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96.)

☐ attorney or agent of record.

☒ attorney or agent acting under 37 CFR 1.34(a).
Registration number if acting under 37 CFR 1.34(a).

Signature

Jane E. R. Potter
Typed or Printed Name

August 19, 2004
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Box 1450, Alexandria, VA 22313-1450.

SEA 1539491v1 59516-147
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,585	07/30/2001	Tian-Qiang Sun	PP-16093.002	2590

7590 10/13/2004

Chiron Corporation
Intellectual Property R338
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

DOCKETED on/by 10/19/04 gm
Atty. CAL PA
File # PP16093.002
Due Date 10/19/04 Ext BA5
Final Date 3/19/05 BA0

Advisory Action	Application No.	Applicant(s)	
	09/919,585	SUN ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 August 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *19 August 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-6*.

Claim(s) withdrawn from consideration: *7-25*.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit: 1652

Continuation of 2. NOTE: Applicants proposed amendment of claim 1 deleting the recitiation of SEQ ID NO: 4 from the claim, if entered would result in further search. Further it appears that applicants amendment deletes the second parenthesis of "(b)" in part (c) which would result in an objection to the claim..

Continuation of 5. does NOT place the application in condition for allowance because: the rejections of record remain based upon the non-entry of applicants proposed amendment.

FACSIMILE COVER SHEET
PTO TECHNOLOGY CENTER 1600

Fax Number (703) 308-0294

FROM: Richard Hutson, Ph.D.

ART UNIT: 1652

SERIAL NO: 09/919,585

TO: Jane Potter

COMPANY:

FAX NUMBER: (206) 628-7699

OF PAGES: 4

(including this page)

IF YOU DO NOT RECEIVE A LEGIBLE COPY OR IF YOU DO NOT RECEIVE ALL OF THE PAGES, PLEASE CALL THE EXAMINER AT (571) 272-0930.

THANK YOU.

Interview Summary	Application No. 09/919,585	Applicant(s) SUN ET AL	
	Examiner Richard G. Hutson	Art Unit 1652	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Richard G. Hutson*. (3)_____.

(2) *Jane Potter*. (4)_____.

Date of Interview: *03 November 2004*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☒ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *all of record*.

Identification of prior art discussed: *none*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *See Continuation Sheet*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR 1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation Sheet (PTOL-413) Application No. 09/919,585

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Applicants representative asked the examiner for an explanation for the advisory that was recently sent to applicants in response to applciants proposed amendment cancelling the subject matter of SEQ ID NO:4 from the claims. The examiner explained that the amendment would not be entered after-final rejection because the entry of such an amendment would necessitate a new/further search. The basis of such is that previously the claims were drawn to those nucleic acid molecules comprising a sequence selected from the group of parts (a) through (k) (i.e. SEQ ID NO: 6, and SEQ ID NO: 4). Because art was found that would read on this genus claim, applciants proposed cancellation of the subject matter of SEQ ID NO: 4 would cause a further search of the newly claimed sub-genus drawn to only the subject matter of SEQ ID NO: 6. As such the amendment will not be entered after-final, but potentially could be entered after filing of a continuation .